

REMARKS

The Office Action mailed August 29, 2002, has been received and reviewed. Claims 1, 2, 4-16 and 22-27 are currently pending in the application. Claims 2, 7-9, 1, 13, 27, 31 and 33-37 currently stand rejected. Applicants have canceled claims 23, 24, 26 and 27 without prejudice or disclaimer and reserve the right to prosecute the claims at a later time. Applicants respectfully request reconsideration of the application as amended herein and in view of the remarks presented below.

I. Priority

Claim 1 was thought to have priority only to 4/15/97 because the prior specification was not thought to provide sufficient written description to support an **apoptin protein**. Applicants would like to make clear that the chicken anemia virus (CAV) nucleic acid encodes three (3) proteins: VP1, VP2 and VP3. The CAV-VP3 protein was later renamed “apoptin.” (See, the specification at page 1, line 3 and lines 11-12). Therefore, CAV-VP3 and apoptin are the same protein. Thus, claim 1 properly does have priority to at least 7/19/94. In addition, the Examiner has noted that “[a] gene delivery vehicle comprising chicken anemia virus protein 2 (VP2) and/or **chicken anemia virus protein 3 (VP3)** only enjoys priority [to] 7/19/94” (Page 15 of the Office Communication (emphasis in original)).

Claims 22-23 and 25-26 are entitled to claim priority to at least 7/19/94, as acknowledged on page 16 of the Office Communication.

The present application hereby claims priority to EP 97201121.7, filed April 15, 1997. Enclosed herewith is a certified copy of the priority document, EP 97201121.7.

II. 35 U.S.C. § 112, First Paragraph

Claims 1, 2, 4-16 and 22-27 were rejected under 35 U.S.C. § 112, first paragraph, as assertedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. Applicants respectfully traverse the rejection.

Claim 1 has been amended to more particularly point out the claimed invention. The amendment does not alter the scope of the claim. It simply clarifies the claim and conforms the language of the claim to the older language or term used in the specification. Support for the amendment can be found, for example, on page 1, lines 11-12 of the specification as filed.

The Applicant would like to make clear that the chicken anemia virus (CAV) nucleic acid encodes three (3) proteins: VP1, VP2 and VP3. The CAV-VP3 protein was later renamed “apoptin.” (See, the specification at page 1, line 3 and lines 11-12). Therefore, CAV-VP3 and apoptin are the same protein. However, to more particularly point out the claimed invention Applicants have amended claim 1 to bring it more in line with the wording of claim 4.

Hence, claims 1, 2, 4-16 and 22-27 do not currently claim a genus of nucleic acid molecules encoding apoptin proteins, but claim a gene delivery vehicle comprising a nucleic acid molecule encoding a chicken virus VP3 protein. Thus, the specification describes the claims such that a person of skill in the art would know that the inventors had possession of the claimed invention at the time of filing. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1, 2, 4-16 and 22-27 were rejected under 35 U.S.C. § 112, first paragraph as assertedly not being enabled commensurate with the scope of the claims. Applicants thank the Examiner for the detailed analysis of the enablement provided in the specification as outlined on page 7 of the Office Action. As noted therein, the specification is enabled for a “gene delivery vector comprising a nucleic acid sequence encoding a chicken anemia virus protein VP3 or the C-terminal 50 amino acids of the VP3 protein.” *Id.* As previously discussed, claims 1, 2 and 4-16 are directed to a gene delivery vehicle comprising a nucleic acid molecule encoding a chicken virus VP3 protein, which is admittedly enabled by the specification. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 23, 24, 26 and 27 have been canceled, mooting the rejection regarding these claims. Applicants have merged the subject matter of claim 23 into claim 22, and merged claim 26 into claim 25. Therefore, claims 22 and 25, as amended, are clearly enabled by the

specification as noted by the Examiner in point 6 of the analysis of enablement (page 8 of the Office Communication). Applicants thus, respectfully request reconsideration and withdrawal of the rejection.

Claims 23-24 and 26-27 were objected to as lacking proper antecedent basis. Claims 23-24 and 26-27 have been canceled without prejudice or disclaimer. Therefore, the objection is mooted by the amendment.

III. 35 U.S.C. § 102(e) Anticipation Rejections

Claims 1, 4, 6, 8, 12, 13, 14, 22, 23, 25 and 26 stand rejected as being anticipated by Noteborn *et al.* (U.S. Patent 6,071,520, effective filing date 7/19/1994).

Claims 1, 4, 6, 8, 12, 13, 14, 22, 23, 25 and 26 are entitled to priority to 7/19/94 as described above in regard to priority, hence U.S. Patent 6,071,520, effective filing date 7/19/1994, is not an effective reference. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. 35 U.S.C. § 103 Obviousness Rejections

Claims 22-27 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Noteborn *et al.* (U.S. Patent 6,071,520, effective filing date 7/19/94) in view of Donehoe *et al.* (U.S. Patent 5,661,126, effective filing date 1/23/93). As noted by the Examiner on page 16 of the Office Communication, claims 22, 23 and 25-26 enjoy priority to 7/19/94. Claims 23, 24, 26 and 27 have been canceled. Claims 22 and 25, as noted by the Examiner, are entitled to priority to 7/19/94. Hence, U.S. Patent 6,071,520 is not an effective reference against the claims. Applicants thus, respectfully request reconsideration and withdrawal of the rejection.

V. Double Patenting

U.S. Patents 6,162,461 and 5,981,502 are assigned to the same party as the application, Leadd B.V., as shown by the assignment recorded on the aforementioned patents and recorded

for the present application, reel number 012828, frame 0373. Therefore, the present application and U.S. Patents 6,162,461 and 5,981,502 are commonly owned by Leadd B.V, and the present inventors were under an obligation to assign the application at the time the invention was made.

Claims 22-23 and 25-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over U.S. Patents. 6,162,461 and 5,981,502.

Claims 1, 4, 6, 8 and 22-23 stand rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over U.S. Patent 6,162,461.

Claims 23-29, 31-33 and 37-41 of U.S. Patent 6,162,461 are directed to a method of inducing apoptosis in a tumor cell, said method comprising: transfecting said cell with an expression vector encoding one or both of a polypeptide depicted in Fig. 3 or Fig. 2. In contrast, claims 1, 4, 6, 8 and 22 are directed to a gene delivery vehicle and a method of using the same. In addition, transfecting a cell with an expression vector is patentably distinct from a gene delivery vehicle. Furthermore, using naked DNA as a gene delivery vehicle is patentably distinct from transfecting a cell.

However, to speed prosecution of the application, Applicants offer to file a terminal disclaimer for claims 22 and 25 in regard to U.S. Patents. 6,162,461

Claims 22-23 and 25-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over U.S. Patent 5,981,502. Claims 23 and 26 have been canceled from the present application. Applicants offer to file a terminal disclaimer for claims 22 and 25 in regard to U.S. Patent 5,981,502 when the claims are found allowable.

Applicants respectfully request reconsideration and withdrawal of the rejection.

V. Noncompliance with 37 C.F.R. §§ 1.821 through 1.825.

The specification is said to be in noncompliance with 37 C.F.R. §§ 1.821 through 1.825, because page 10 lists nucleotide sequences, but does not list a SEQ ID NO for each nucleotide sequence. The applicants' attorney has reviewed page 10 of the present application and the Applicants response to the Notice to Comply mailed to the office on November 28, 2001.

Applicants responded by replacing the paragraph beginning on page 10, line 3 and ending on page 10, line 16 and inserting SEQ ID NOs:1 and 2 following the nucleotide sequences included therein. Specifically, this paragraph should now have the sequence (5'-GGGTGGAGTTGTGACGTG-3') identified as SEQ ID NO:1 and the sequence (5'-TCGTGAAGGGTAGGTGGTTC-3') identified as SEQ ID NO:2.

However, to the extent that the amendment to the paragraph was not entered previously Applicants herein have replaced the paragraph so as to ensure proper reference to the SEQ ID NOs for each nucleotide sequence.

VI. Objection to the Drawings filed on October 14, 1999.

Correction of Informalities under 37 C.F.R. § 1.85 will be submitted

VII. Information Disclosure Statement.

In compliance with the duty to disclose information and in conformity with MPEP § 609A(1) an Information Disclosure Statement is submitted herewith.

Conclusion

In view of the foregoing amendments, and further in view of the arguments made, it is believed that the application is now in condition for allowance. If any questions remain the Examiner is respectfully requested to call Applicants representative at the number provided herein.

Respectfully submitted,



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Date: November 29, 2002

GSD/gsd

Document (#22194) in ProLaw

Marked up version showing changes made

IN THE SPECIFICATION:

The paragraph on page 10, lines 3-16 is to be replaced with the paragraph below, which shows the changes made.

The 911 and PER.C6 produced rAdV stocks were screened for the presence of recombinant-competent adenovirus by performing PCR analysis with primers derived from the Ad5 ITR region (5[]'-GGGTGGAGTTGTGACGTG-3[]) SEQ ID NO:1 and the E1A encoding region (5[]'-TCGTGAAGGGTAGGTGGTTC-3[]) SEQ ID NO:2 as described by Noteborn and De Boer (1995) using a Perkin Elmer PCRapparatus. The presence of a 600-bp amplified fragment indicates that replication-competent (El-region containing) adenovirus exists in the [analysed] analyzed virus stock (Hoeben, unpublished results) or by infecting HepG2 cells with rAdV batch. During a period of at least 10 days, the cells were monitored for potential cytopathogenic effects and by indirect immunofluorescence using a specific monoclonal antiserum directed against ElA protein.

IN THE CLAIMS:

1. (Twice amended) A gene delivery vehicle comprising a nucleic acid molecule encoding [apoptin protein.] a chicken anemia virus protein VP3.
4. (Amended) A gene delivery vehicle comprising a nucleic acid molecule encoding a chicken anemia virus protein VP2.
14. (Amended) A host cell comprising [a] the gene delivery vehicle according to claim 13.
22. (Amended) A method for inducing apoptosis in a mammalian tumor by directly administering the gene delivery vehicle of claim 1 to a mammal.

25. (Amended) A method for inducing apoptosis in a mammalian tumor by directly administrating the gene delivery vehicle of claim 6 to a mammal.